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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main

Statistical parameters

text	, or i	vietnods section).
n/a	Cor	nfirmed
	\boxtimes	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
	\boxtimes	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
		The statistical test(s) used AND whether they are one- or two-sided Only common tests should be described solely by name; describe more complex techniques in the Methods section.
	\boxtimes	A description of all covariates tested
	\boxtimes	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	\boxtimes	A full description of the statistics including <u>central tendency</u> (e.g. means) or other basic estimates (e.g. regression coefficient) AND <u>variation</u> (e.g. standard deviation) or associated <u>estimates of uncertainty</u> (e.g. confidence intervals)
	\boxtimes	For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
\boxtimes		For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
\boxtimes		For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
	\boxtimes	Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated
		Clearly defined error bars State explicitly what error bars represent (e.g. SD, SE, CI)

Our web collection on $\underline{statistics\ for\ biologists}$ may be useful.

Software and code

Policy information about availability of computer code

Data collection

Cell Quest Pro (BD) FACS Diva (BD) Cytoflex (BC)

AxioVision (r4.8.2, Carl Zeiss MicroImaging)

VS-ASW (Olympus Corp)

Zen 2011 SP3 (Carl Zeiss) v8.1.11.484

MRI (see below)

OneStep real-time PCR (Applied Biosystems) - v2.3

Magellan (Tecan) - v6.6

MicroBeta TriLux (PerkinElmer Life Sciences)

BZ-II Analyzer Software (Keyence)

Data		

- FIJI image processing software (NIH) v2.0.0-rc-59/1.51n
- Imaris (Bitplane) v8.0.1
- FlowJo (FlowJo LLC) v.10
- Prism (GraphPad Software, Inc) v7.0a
- Excel (MicrosoftOffice 2010, v14.0.7208.5000)
- CytExpert (v 2.3 BC)

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The data will be available without restriction

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Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.				
☐ Life sciences	Behavioural & social sciences	Ecological, evolutionary & environmental sciences		
or a reference copy of the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf				

Life sciences study design

All studies filust dis	ciose on these points even	i when the disclosure is nego	auve.	

Sample size Sample sizes were chosen on the basis of standard power calculations (with α = 0.05 and power of 0.8) performed for similar experiments that were previously published. In general, statistical methods were not used to re-calculate or predetermine sample sizes.

Data exclusions No samples were excluded from the analysis.

Replication Number of reliable reproductions of each experimental finding is stated in each figure legend.

Randomization Animals from different cages, but within the same

experimental group, were selected to assure randomization.

Blinding Reported in METHODS

Timing

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description Briefly describe the study type including whether data are quantitative, qualitative, or mixed-methods (e.g. qualitative cross-sectional,

quantitative experimental, mixed-methods case study).

Research sample

State the research sample (e.g. Harvard university undergraduates, villagers in rural India) and provide relevant demographic information (e.g. age, sex) and indicate whether the sample is representative. Provide a rationale for the study sample chosen. For studies involving

existing datasets, please describe the dataset and source.

Sampling strategy

Describe the sampling procedure (e.g. random, snowball, stratified, convenience). Describe the statistical methods that were used to

Describe the sampling procedure (e.g. random, snowball, stratified, convenience). Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient. For qualitative data, please indicate whether data saturation was considered, and what criteria were used to decide that no further sampling was needed.

Provide details about the data collection procedure, including the instruments or devices used to record the data (e.g. pen and paper, computer, eye tracker, video or audio equipment) whether anyone was present besides the participant(s) and the researcher, and whether the researcher was blind to experimental condition and/or the study hypothesis during data collection.

Indicate the start and stop dates of data collection. If there is a gap between collection periods, state the dates for each sample cohort.

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Data exclusions

If no data were excluded from the analyses, state so OR if data were excluded, provide the exact number of exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.

Non-participation

State how many participants dropped out/declined participation and the reason(s) given OR provide response rate OR state that no participants dropped out/declined participation.

Randomization

If participants were not allocated into experimental groups, state so OR describe how participants were allocated to groups, and if allocation was not random, describe how covariates were controlled.

Ecological, evolutionary & environmental sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description

Briefly describe the study. For quantitative data include treatment factors and interactions, design structure (e.g. factorial, nested, hierarchical), nature and number of experimental units and replicates.

Research sample

Describe the research sample (e.g. a group of tagged Passer domesticus, all Stenocereus thurberi within Organ Pipe Cactus National Monument), and provide a rationale for the sample choice. When relevant, describe the organism taxa, source, sex, age range and any manipulations. State what population the sample is meant to represent when applicable. For studies involving existing datasets, describe the data and its source.

Sampling strategy

Note the sampling procedure. Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.

Data collection

Describe the data collection procedure, including who recorded the data and how.

Timing and spatial scale

Indicate the start and stop dates of data collection, noting the frequency and periodicity of sampling and providing a rationale for these choices. If there is a gap between collection periods, state the dates for each sample cohort. Specify the spatial scale from which the data are taken

Data exclusions

If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.

Reproducibility

Describe the measures taken to verify the reproducibility of experimental findings. For each experiment, note whether any attempts to repeat the experiment failed OR state that all attempts to repeat the experiment were successful.

Randomization

Describe how samples/organisms/participants were allocated into groups. If allocation was not random, describe how covariates were controlled. If this is not relevant to your study, explain why.

Blinding

Describe the extent of blinding used during data acquisition and analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study.

Did the study involve field work?

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Field work, collection and transport

Field conditions

Describe the study conditions for field work, providing relevant parameters (e.g. temperature, rainfall).

Location

State the location of the sampling or experiment, providing relevant parameters (e.g. latitude and longitude, elevation, water depth).

Access and import/export

Describe the efforts you have made to access habitats and to collect and import/export your samples in a responsible manner and in compliance with local, national and international laws, noting any permits that were obtained (give the name of the issuing authority, the date of issue, and any identifying information).

Disturbance

Describe any disturbance caused by the study and how it was minimized.

Reporting for specific materials, systems and methods

Materials & experimental sy	vstems Methods				
n/a Involved in the study	n/a Involved in the study				
Unique biological materia	als ChIP-seq				
Antibodies	Flow cytometry				
Eukaryotic cell lines	MRI-based neuroimaging				
Palaeontology					
Animals and other organi					
Human research particip	ants				
Unique biological ma	aterials				
Policy information about available					
Obtaining unique materials	Describe any restrictions on the availability of unique materials OR confirm that all unique materials used are readily available from the authors or from standard commercial sources (and specify these sources).				
Antibodies					
Antibodies used	Reported in METHODS				
Antibodies used	neported in Michaels				
Validation	Describe the validation of each primary antibody for the species and application, noting any validation statements on the manufacturer's website, relevant citations, antibody profiles in online databases, or data provided in the manuscript.				
Eukaryotic cell lines					
Policy information about <u>cell lin</u>	<u>es</u>				
Cell line source(s)	GP+E86 ecotropic retroviral packaging cell line (ATCC). Lewis rat CD4 effector T cell lines specific for myelin basic protein (this study). Lewis rat CD4 effector T cell lines specific for beta-synuclein (this study). Lewis rat CD4 effector T cell lines specific for ovalbumin (this study).				
Authentication	No authentication was performed for GP+E86 and derivative cell lines. For T cell lines, authentication reported in METHODS. For T cell lines characterization see Ext Data Fig. 1				
Mycoplasma contamination	All used cell lines were tested negative for mycoplasma contamination.				
Commonly misidentified lines (See <u>ICLAC</u> register)	Name any commonly misidentified cell lines used in the study and provide a rationale for their use.				
Palaeontology					
	Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the				
Specimen provenance	issuing authority, the date of issue, and any identifying information).				
Specimen deposition	Indicate where the specimens have been deposited to permit free access by other researchers.				
Dating methods	If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement),				
	where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.				
Tick this box to confirm th	at the raw and calibrated dates are available in the paper or in Supplementary Information.				
Animals and other o	rganisms				
Policy information about studie	s involving animals; ARRIVE guidelines recommended for reporting animal research				
Laboratory animals	Lewis rats on a LEW/Crl background were bred at the animal facility of the University Medical Centre Göttingen (Germany) or obtained from Charles River (Germany). T cell receptor transgenic Lewis rat strain (ubiquitous expression of GFP-TCRa-TCRb				

transgene; unknown integration site) specific for beta-synuclein antigen was generated in this study and maintained at theanimal facility of University Medical Centre Göttingen.

Wild animals

Provide details on animals observed in or captured in the field; report species, sex and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.

Field-collected samples

For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.

Human research par	ticipants			
Policy information about <u>studie</u>	es involving human research participants			
Population characteristics Described in the text (Ext. Data. Fig.10)				
Recruitment	The patients were recruited by a clinician in a random way			
ChIP-seq				
Data deposition				
Confirm that both raw and	d final processed data have been deposited in a public database such as <u>GEO</u> .			
Confirm that you have de	posited or provided access to graph files (e.g. BED files) for the called peaks.			
Data access links May remain private before publication	For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.			
Files in database submission	Provide a list of all files available in the database submission.			
Genome browser session (e.g. <u>UCSC</u>)	Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.			
Methodology				
Replicates	Describe the experimental replicates, specifying number, type and replicate agreement.			
Sequencing depth	Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.			
Antibodies	Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.			
Peak calling parameters	Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.			
Data quality	Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.			
Software	Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.			
Flow Cytometry				
Plots				
Confirm that:				
The axis labels state the m	narker and fluorochrome used (e.g. CD4-FITC).			
The axis scales are clearly	visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).			

All plots are contour plots with outliers or pseudocolor plots. A numerical value for number of cells or percentage (with statistics) is provided. Methodology

Cell population abundance

Sample preparation Reported in Methods BD FACSCalibur, BD FACS Aria II, Cytoflex Instrument Software CellQuest Pro, CytExpert or BD FACS Diva software were used for acquisition of flow cytometry data

> Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.

	ribe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell ulation, indicating where boundaries between "positive" and "negative" staining cell populations are defined.				
Tick this box to confirm that a	figure exemplifying the gating strategy is provided in the Supplementary Information.				
Magnetic resonance im	aging				
Experimental design					
Design type	'Described in the respective Figure legends and the Method section				
Design specifications	not applicable				
Behavioral performance measures	not applicable				
Acquisition					
Imaging type(s)	structural				
Field strength	9.4 T				
Sequence & imaging parameters	T2-weighted axial MRI with repetition time (TR) of 9286 ms, echo time (TE) of 11 ms, RARE factor of 12, 60 slices, in-plane resolution of $120\times120~\mu m$, slice thickness of 480 μm , and total acquisition time (TA) of 195 s as well as sagittal MRI (TR/TE = 4333/11 ms, RARE factor = 12, 28 slices, field-of-view = 30.72×30.72 mm, matrix size = 256×256 , in-plane resolution = $120\times60~\mu m$, slice thickness = $480~\mu m$, and TA = 182 s) were performed with the use of multislice fast spin-echo MRI. T1-weighted fat-suppressed sagittal gradient-echo MRI (3D FLASH, TR/TE = $14.8/4.2$ ms, flip angle = 25° , and TA = 16 min) was performed at an isotropic resolution of $120~\mu m$ (field-of-view = $30.72\times30.72\times30.72\times30.72$ mm, matrix size = 256×256) before and after an intravenous injection of Gadobutrol solution.				
Area of acquisition	Brain				
Diffusion MRI Used	Not used ■ Not used				
Preprocessing					
Preprocessing software	not applicable				
Normalization	not applicable				
Normalization template	not applicable				
Noise and artifact removal	not applicable				
Volume censoring	at applicable				
statistical modeling & inference					
Model type and settings	not applicable				
Effect(s) tested	not applicable				
Specify type of analysis: Who	ole brain 🔀 ROI-based 🔲 Both				
Statistic type for inference (See Eklund et al. 2016)	not applicable				
Correction	not applicable				
Models & analysis					
n/a Involved in the study Functional and/or effective of Graph analysis Multivariate modeling or pre					
Functional and/or effective connec	Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).				

Graph analysis

Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).

Multivariate modeling and predictive analysis

Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.